International Plasma Products Industry Association

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Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Comments on FDA's Guidance for Industry – Revised Precautionary Measures to Reduce Possible Risk of Transmission of Creutzfelt-Jakob Disease and New Variant Creutzfelt-Jakob Disease by Blood and Blood Products

Introduction

The International Plasma Products Industry Association is the trade association representing the major commercial plasma-derivative manufacturers including Alpha Therapeutics, Baxter Healthcare, Bayer Corporation, and Centeon, LLC. Our members produce approximately 80 percent of the plasma derivatives for the U.S. market. IPPIA is pleased to provide these comments on the Food and Drug Administration's recently revised guidance to industry addressing precautionary measures to reduce the risk of transmission of Creutzfelt-Jakob Disease (CJD) in blood and blood products (The Guide).

As agency officials have acknowledged, the nation's blood supply is as safe as it has ever been. Nonetheless, industry, government, and the public must be ever vigilant for potential threats to the blood supply. As such, IPPIA applauds the FDA's goals of striving to maintain a safe blood supply by proactively addressing

potential risks, including theoretical risks such as CJD and new variant CJD (nvCJD).

While we believe it is appropriate for the FDA to develop policies aimed at further reducing potential threats to the blood supply, it is also important that FDA adhere to administrative procedures including public notice and comment. For cases that involve theoretical threats, adherence to these policies becomes even more important. In these cases, the agency must weigh the real effects of responding to theoretical risks against the perceived benefit from those actions. Regarding nvCJD, the agency must weigh a real reduction in supply versus the unknown and unquantifiable reduction in the theoretical risk of transmission of nvCJD through blood and blood products. In order to maintain public confidence in the blood supply, these decisions must be developed through public discussions involving all interested parties and be based on sound scientific reasoning.

Proper Role of FDA Advisory Committees

Federal agencies such as the FDA and the Department of Health and Human Services (HHS) have the authority to bring issues of public policy before an advisory committee. The FDA obtains advice on many topics through several federal advisory committees including the Transmissible Spongiform Encephalopathy (TSE) Advisory Committee, the Blood Products Advisory Committee (BPAC) and the HHS Advisory Committee on Blood Safety and Availability (ACBSA). This process allows the agency to benefit from information and perspectives that would otherwise be unattainable if the agency had to rely solely on agency personnel for this input. Additionally, advisory committee meetings are open to the public, and therefore offer an excellent opportunity to provide for public input into the policy making process. While the use of such committees can provide the FDA with valuable input, it is important to know the limitations of any individual committee. Federal advisory committees should only

be used to deal with issues of science or policy directly related to their mandate and their members' expertise.

The issue raised in the Guide did not receive full review by all available blood safety committees. The FDA, rather than seeking advice from all its various advisory panels, tried to combine this discussion into one meeting by adding several temporary voting members, including two from BPAC, to the TSE Advisory Committee. However, this ad hoc arrangement only served to further confuse the issue and the resulting decision.

While the TSE committee narrowly voted to impose deferral criteria based on time spent in the UK, both BPAC members voted against such a recommendation. The issue, and all the other issues raised in the Guide, such as donor questions, product retrieval, and labeling requirements were never brought before the full BPAC for a vote, nor brought before the HHS ACBSA. Both these committees have mandates to consider varied aspects of this important issue. BPAC's mandate is to consider blood regulatory policy, while the ACBSA's mandate is to consider the safety of the blood supply along with availability and other societal issues. Because each committee is comprised of participants capable of providing advice on these topics, and because these discussions are open public forums, we believe input from these committees may have provided a measured and clear decision on the content on the Guide.

While this process may have been longer, we believe that an issue as important as this, with an enormous potential to affect both the supply and the public confidence in the US blood supply, deserves this type of open and public debate. This is especially true because this issue involves "question of theoretical risk in the absence of sufficient knowledge on which to base any firm conclusion". (Statement of TSE Committee Chair Dr. Paul Brown).

Specific Comments on CJD Guidance

Donor Deferral and Product Disposition

As stated above, IPPIA believes that the process used by the agency to arrive at the decision to defer donors who have spent more than 6 months in the United Kingdom between 1980 and 1996 was flawed. Additionally, because of the theoretical nature of the CJD risk, we believe that no imminent public health concern exists that justifies truncating the public comment process by mandating immediate implementation of the CJD Guide. Consequently, IPPIA requests that FDA withdraw the CJD Guide and reissue it in draft format to permit an adequate opportunity for public input.

Labeling Recommendations

1) Labeling Recommendations for Non-Implicated Plasma-Derived Products:

   IPPIA supports the following statement for all plasma derivatives:

   > (Product Name) is made from human plasma. Therapies made from human plasma may contain a risk of transmitting infectious agents, such as viruses. The risk that (product name) will transmit an infectious agent has been reduced by effective donor screening, manufacturing technologies and viral inactivation/elimination procedures. There is also a theoretical risk that other infectious agents including those not yet known or identified may be present in such therapies.

Rationale:

A) Single Statement

The CJD Guide recommends manufacturers use a different statement for albumin than for the other plasma-derived products. The risk of transmitting CJD and nvCJD through blood and plasma-derived products is theoretical. (Guide at 4 and 5). We believe trying to define degrees of theoretical risk is not justified given the current state of the scientific knowledge of this disease.

Therefore we propose that one general statement be used for all plasma-derived products.

B) Specific Classical CJD Warning

The Guide also recommends that the statement specifically mention "the Creutzfelt-Jakob disease (CJD) agent". However, similar to our argument that defining degrees of theoretical risk is not justified given the current state of the scientific knowledge, we also believe that signaling out one theoretical risk to include on product labeling is not justified. IPPIA supports a general warning that would include all risks from transmissible agents, both known and unknown, as outlined in our statement listed above.

The IPPIA statement is preferable for two reasons. First, it highlights all unknown risks and does not require revision of product labels each time a new theoretical risk is hypothesized. More importantly, this general language does not lead to confusion about the current state of scientific knowledge of any particular theoretical risk. Plasma derivatives are important life saving and life enhancing therapeutics for patients who require them. Mandating warnings of specific theoretical risks will only serve to cause unnecessary concern regarding the administration of these products without adequate scientific proof to justify those concerns.

Currently, the available scientific evidence indicates "that transmission of the [classical] CJD infectious agent by blood products is highly unlikely". (Guide at page 2). Based on this FDA statement, inclusion of the specific theoretical risk of classical CJD transmission on product labeling is unjustified.

C) Specific nvCJD Warning

Regarding nvCJD, the Guide states "the transmissibility of nvCJD by blood or blood products is unknown" (Guide at 4). The guide further states "Until more

is known about the possibility of nvCJD transmission by blood components or plasma derivatives, a precautionary policy of withdrawal for all of these products is recommended for material from donors with nvCJD" (Id at 4-5). IPPIA fully supports the FDA's precautionary policy of withdrawing products containing material from a donor subsequently diagnosed with nvCJD. However, precautionary policies based on the lack of any scientific evidence do not justify signaling out the nvCJD agent for inclusion on product labels. Mentioning the nvCJD agent sets a precedent to require a listing of all theoretical risks, regardless of the scientific evidence to support them.

2) Labeling requirements for Products Containing Albumin:

Based on the above discussion IPPIA supports the following statement for all products containing albumin:

(Product Name) contains albumin, a derivative of human plasma. Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that albumin will transmit an infectious agent has been reduced by effective donor screening, product manufacturing technologies and viral inactivation/elimination procedures. There is also a theoretical possibility that infectious agents not yet known or identified may be present in such products.

Conclusion

IPPIA appreciates the opportunity to comment on this important guidance. Although the nation's blood supply is safe, we recognize the need to be vigilant about potential threats. However, actions taken to address potential threats must be carefully balanced against the impact of such actions. In these instances, adherence to administrative procedures, and the opportunity for public comment, provide stakeholder involvement in the decision-making process and ultimately ensure confidence in any ensuing policy. For these reasons, and those

discussed above, we urge the FDA to withdraw the Guide and reissue it as a draft with more opportunity for stakeholder involvement with this important issue.

Sincerely,

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